

## **AMENDMENTS TO THE CLAIMS**

Please amend the claims as follows. This listing of claims will replace all prior versions, and listings, of claims in the applications:

### **Listing of Claims:**

Claims 1-232 (canceled)

233. (previously presented) A polynucleotide encoding a protein consisting of

the extracellular region of an insoluble human tumor necrosis factor (TNF) receptor, wherein said insoluble human TNF receptor (a) has an apparent molecular weight of about 75 kilodaltons as determined on a non-reducing SDS-polyacrylamide gel, (b) is encoded by a nucleic acid having the same sequence as a nucleic acid from a cDNA library made from an extract of an HL-60 cell culture (American Type Culture Collection, Manassas, VA, deposited under ATCC No. CCL240), and (c) comprises the amino acid sequence LPAQVAFXPYAPEPGSTC (SEQ ID NO: 10), and

all of the domains of the constant region of a human immunoglobulin IgG heavy chain other than the first domain of said constant region,

wherein the protein specifically binds human TNF.

234. (previously presented) A polynucleotide of claim 233 wherein said insoluble human TNF receptor protein further comprises the amino acid sequences LCAP (SEQ ID NO: 12), VFCT (SEQ ID NO: 8), NQPQAPGVEASGAGEA (SEQ ID NO: 9) and VPHLPAD (SEQ ID NO: 13).

235. (previously presented) The polynucleotide of claim 234, wherein the IgG heavy chain is an IgG<sub>1</sub> heavy chain.

236. (currently amended) The polynucleotide of claim 233, wherein all of the domains of the constant region of a human immunoglobulin IgG heavy chain other than the first domain of said constant region consist essentially of the immunoglobulin amino acid

sequence encoded by the DNA sequence of ~~pCD4Hy1~~ pCD4-Hy1 vector (deposited at Deutschen Sammlung von Mikroorganismen und Zellkulturen GmbH (DSM) in Braunschweig, FRG under No. DSM 5314) or of pCD4-Hy3 vector (deposited at Deutschen Sammlung von Mikroorganismen und Zellkulturen GmbH (DSM) in Braunschweig, FRG under No. DSM 5523).

237. (currently amended) The polynucleotide of claim 236, wherein all of the domains of the constant region of a human immunoglobulin IgG heavy chain other than the first domain of said constant region consist essentially of the immunoglobulin amino acid sequence encoded by the DNA sequence of ~~pCD4Hy1~~ pCD4-Hy1 vector (deposited at Deutschen Sammlung von Mikroorganismen und Zellkulturen GmbH (DSM) in Braunschweig, FRG under No. DSM 5314).

238. (canceled)

239. (previously presented) A vector comprising the polynucleotide of claim 235.

240. (previously presented) A host cell comprising the polynucleotide of claim 235.

241. (currently amended) A method of producing a protein that specifically binds human TNF, comprising the steps of:

(a) culturing ~~the~~ a host cell comprising the polynucleotide of claim 235 of ~~claim 240~~ and

(b) purifying the expressed protein encoded by the polynucleotide ~~that~~ specifically binds human TNF from the cell mass or the culture medium.

242. (previously presented) The method of claim 241, wherein the host cell is a CHO cell.

243. (previously presented) A polynucleotide encoding a protein consisting of

the extracellular region of the human p75 TNF receptor amino acid sequence encoded by the cDNA insert of the plasmid deposited with the American Type Culture Collection (ATCC) on October 17, 2006 under Accession No. PTA 7942, and

all of the domains of the constant region of a human immunoglobulin IgG heavy chain other than the first domain of said constant region,

wherein the protein specifically binds human TNF.

244 – 245. (canceled)

246. (previously presented) The polynucleotide of claim 243, wherein the IgG heavy chain is an IgG<sub>1</sub> heavy chain.

247. (currently amended) The polynucleotide of claim 246, wherein all of the domains of the constant region of a human immunoglobulin IgG heavy chain other than the first domain of said constant region consist essentially of the immunoglobulin amino acid sequence encoded by the DNA sequence of ~~pCD4H $\gamma$ 1~~ pCD4-H $\gamma$ 1 vector (deposited at Deutschen Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) in Braunschweig, FRG under No. DSM 5314) or of pCD4-H $\gamma$ 3 vector (deposited at Deutschen Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) in Braunschweig, FRG under No. DSM 5523).

248. (currently amended) The polynucleotide of claim 247, wherein all of the domains of the constant region of a human immunoglobulin IgG heavy chain other than the first domain of said constant region consist essentially of the immunoglobulin amino acid sequence encoded by the DNA sequence of ~~pCD4H $\gamma$ 1~~ pCD4-H $\gamma$ 1 vector (deposited at Deutschen Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) in Braunschweig, FRG under No. DSM 5314).

249. (previously presented) A vector comprising the polynucleotide of claim 246.

250. (previously presented) A host cell comprising the polynucleotide of claim 246.

251. (currently amended) A method of producing a protein that specifically binds human TNF, comprising the steps of:

(a) culturing ~~the~~ a host cell comprising the polynucleotide of claim 246 ~~of claim 250~~ and

(b) purifying the expressed protein encoded by the polynucleotide ~~that specifically binds human TNF~~ from the cell mass or the culture medium.

252. (previously presented) The method of claim 251, wherein the host cell is a CHO cell.

253. (previously presented) A polynucleotide encoding a protein consisting of

the extracellular region of an insoluble human TNF receptor, wherein said insoluble human TNF receptor has the amino acid sequence of the insoluble receptor of SEQ ID NO:27, and

all of the domains of the constant region of a human immunoglobulin IgG heavy chain other than the first domain of said constant region,

wherein the protein specifically binds human TNF.

254. (canceled)

255. (previously presented) The polynucleotide of claim 253, wherein the IgG heavy chain is an IgG<sub>1</sub> heavy chain.

256. (currently amended) The polynucleotide of claim 253, wherein all of the domains of the constant region of a human immunoglobulin IgG heavy chain other than the first domain of said constant region consist essentially of the immunoglobulin amino acid sequence encoded by the DNA sequence of ~~pCD4Hy1~~ pCD4-Hy1 vector (deposited at

Deutschen Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) in Braunschweig, FRG under No. DSM 5314) or of pCD4-Hy3 vector (deposited at Deutschen Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) in Braunschweig, FRG under No. DSM 5523).

257. (currently amended) The polynucleotide of claim 256, wherein all of the domains of the constant region of a human immunoglobulin IgG heavy chain other than the first domain of said constant region consist essentially of the immunoglobulin amino acid sequence encoded by the DNA sequence of ~~pCD4-Hy1~~ pCD4-Hy1 vector (deposited at Deutschen Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) in Braunschweig, FRG under No. DSM 5314).

258. (previously presented) A vector comprising the polynucleotide of claim 255.

259. (previously presented) A host cell comprising the polynucleotide of claim 255.

260. (currently amended) A method of producing a protein that specifically binds human TNF, comprising the steps of:

(a) culturing ~~the~~ a host cell comprising the polynucleotide of claim 255 ~~of claim 259~~, and

(b) purifying the expressed protein encoded by the polynucleotide ~~that specifically binds human TNF~~ from the cell mass or the culture medium.

261. (previously presented) The method of claim 260, wherein the host cell is a CHO cell.

262 – 273. (canceled)

274. (currently amended) A method of producing a ~~recombinantly expressed~~ protein that specifically binds human TNF, comprising the steps of:

- (a) culturing a host cell comprising a polynucleotide, wherein the polynucleotide encodes the  $\alpha$ - protein and wherein the protein consists consisting of:
  - (i) the extracellular region of an insoluble human TNF receptor, wherein the insoluble human TNF receptor has an apparent molecular weight of about 75 kilodaltons as determined on a non-reducing SDS-polyacrylamide gel and comprises the amino acid sequence LPAQVAFXPYAPEPGSTC (SEQ ID NO: 10), and
  - (ii) all of the domains of the constant region of a human IgG immunoglobulin heavy chain other than the first domain of said constant region, and
- (b) purifying the ~~recombinantly-expressed~~ protein from the cell mass or the culture medium.

275. (previously presented) The method of claim 274, wherein the host cell is a CHO cell.

276. (previously presented) The method of claim 274, wherein the IgG heavy chain is an IgG<sub>1</sub> heavy chain.

277. (previously presented) A polynucleotide encoding a protein consisting of:

- (a) the extracellular region of an insoluble human TNF receptor,
 

wherein the insoluble human TNF receptor (i) has an apparent molecular weight of about 75 kilodaltons as determined on a non-reducing SDS-polyacrylamide gel and (ii) comprises the amino acid sequence LPAQVAFXPYAPEPGSTC (SEQ ID NO: 10), and
- (b) all of the domains of the constant region of a human IgG<sub>1</sub> immunoglobulin heavy chain other than the first domain of said constant region.

278. (previously presented) A vector comprising the polynucleotide of claim 277.

279. (previously presented) A mammalian host cell comprising the polynucleotide of claim 277.

280. (currently amended) A method of producing a ~~recombinantly expressed~~ protein, comprising the steps of:

- (a) culturing a host cell comprising a polynucleotide, wherein the polynucleotide encodes the  $\alpha$ -protein and wherein the protein consists consisting of:
  - (i) the extracellular region of an insoluble human TNF receptor, wherein the insoluble human TNF receptor comprises the amino acid sequence of SEQ ID NO:27 and
  - (ii) all of the domains of the constant region of a human IgG immunoglobulin heavy chain other than the first domain of said constant region, and
- (b) purifying the ~~recombinantly expressed~~ protein from the cell mass or the culture medium.

281. (previously presented) The method of claim 280, wherein the human IgG immunoglobulin heavy chain is an IgG<sub>1</sub> heavy chain.

282. (previously presented) The method of claim 280, wherein the host cell is a CHO cell.

283. (previously presented) The method of claim 281, wherein the host cell is a CHO cell.

284. (new) A method of producing a protein, comprising the steps of:

- (a) culturing a host cell comprising a polynucleotide, wherein the polynucleotide encodes the protein and wherein the protein consists of:
  - (i) a TNF-binding soluble fragment of an insoluble human TNF receptor, wherein the insoluble human TNF receptor comprises the amino acid sequence of SEQ ID NO:27 and
  - (ii) all of the domains of the constant region of a human IgG<sub>1</sub> immunoglobulin heavy chain other than the first domain of said constant region, and
- (b) purifying the protein from the cell mass or the culture medium.

285. (new) A method of producing a protein, comprising the steps of:

- (a) culturing a host cell comprising a polynucleotide, wherein the polynucleotide encodes the protein and wherein the protein consists of:
  - (i) a TNF-binding soluble fragment of the human p75 TNF receptor amino acid sequence encoded by the cDNA insert of the plasmid deposited with the American Type Culture Collection (ATCC) on October 17, 2006 under Accession No. PTA 7942 and
  - (ii) all of the domains of the constant region of a human IgG<sub>1</sub> immunoglobulin heavy chain other than the first domain of said constant region, and
- (b) purifying the protein encoded from the cell mass or the culture medium.

286. (new) A method of producing a protein, comprising the steps of:

- (a) culturing a host cell comprising a polynucleotide, wherein the polynucleotide encodes the protein and wherein the protein consists of:
  - (i) a TNF-binding soluble fragment of an insoluble human TNF receptor, wherein the insoluble human TNF receptor has an apparent molecular weight of about 75 kilodaltons as determined on a non-



reducing SDS-polyacrylamide gel and comprises the amino acid sequence LPAQVAFXPYAPEPGSTC (SEQ ID NO: 10) and

(ii) all of the domains of the constant region of a human IgG<sub>1</sub> immunoglobulin heavy chain other than the first domain of said constant region, and

(b) purifying the protein encoded from the cell mass or the culture medium.